Point Prevalence Surveys of Health Care Associated Infections: A Systematic Review

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Abstract

Healthcare associated infections (HAIs) are considered as a serious public health issues that contribute substantially to the global burden of mortality and morbidity with respect to infectious diseases. The aim is to assess the burden of healthcare associated infections by collation of available data from published point prevalence surveys (PPS) on HAIs to give future guidance. Study protocol and methodology was designed according to preferred reporting items for systematic reviewsand meta-analysis (PRISMA) guidelines. Published research papers that conducted point prevalence survey of HAIs in hospital settings by following the structured survey methodology employed by European Centre of Disease Prevention and Control (ECDC) were included. Of 1212 articles, 67 studies were included in the final analysis conducted across different countries. Overall, 35 studies were conducted in Europe, 21 in Asia, 9 in America, and 2 in Africa. The highest prevalence of HAIs was recorded in a study conducted in adult ICU settings of 75 regions of Europe (51.3%). The majority of the studies included HAI data on urinary tract infections, respiratory tract infections and bloodstream infections. *Klebseilla pneumonia*, *Pseudomonas aeruginosa* and *E. coli* were the most frequent pathogens responsible for HAIs. PPS is useful tool to quantify HAIs and provides a robust baseline data for policy makers. However, a standardize surveillance method is required. In order to minimize the burden of HAIs, infection prevention and control programs and antibiotic stewardship may be effective strategies to minimize risk of HAIs.

Keywords: Point prevalence surveys, Healthcare associated infections, Hospital, Infection presentation and control.

1. INTRODUCTION

Globally, healthcare-associated infections (HAIs) are considered as a major health and economic burden, with a resultant increase in the length of hospitalization, morbidity and mortality amongst hospitalized patients [1-4]. Overall, HAIs are considered as the most adverse event in healthcare delivery [5]. Surveillance of HAIs is an integral component of any comprehensive infection prevention and control (IPC) program, which provides information that are necessary to highlight and address challenging areas [6-9]. Point-prevalence surveys (PPS) have been used for the surveillance of HAI for many years [10]. The pioneering project started in the 1970s by the US Centers for Disease Control and Prevention (CDC) who used repeated PPS to investigate the advantage of establishing IPC teams in US hospitals [6]. In Europe, HAI surveillance and infection prevention and control programs are coordinated by the European Centre for Disease Prevention and Control (ECDC). PPS is a time and cost effective method which estimates the burden of HAIs and related risk factors, especially in hospitals with limited resources [11-14]. However going forward, a more resource demanding and cumbersome program, i.e., prospective incidence surveillance, may be needed especially in high-risk specialties to help prevent HAIs [15, 16].

Whilst the exact global burden of HAI is unknown, estimated prevalence rates are between 5.7%-19.1% among low and middle income countries (LMICs) and 5.7% - 7.5% in high income countries [17, 18]. However, rates up to 28% to 45.8% have been reported in sub-Saharan African countries depending on the country and the ward surveyed [19, 20]. In 2002, the Centers for Disease Control and Prevention (CDC) reported approximately 1.7 million cases of HAIs in US hospitals [21]. In 2012, a literature review performed by ECDC documented that over 3.2 million patients acquire at least one HAI in Europe every year with 16 million extra days of hospitalization and 37,000 attributable deaths [22]. The revised European Annual Epidemiological Report (AER) published in 2008 reported that the overall annual burden of direct annual financial losses due to HAIs were estimated at approximately €7 billion [22-24]. IPC strategies provide cost-effective solutions as 20–30 % of HAI are avoidable [25, 26]. However, as mentioned, the risks of HAIs appear considerably higher in LMICs including sub-Sahara Africa, and the impact on patients and health-care systems is considerable and typically greatly under estimated [19, 20, 27-29]. This is a concern as HAIs increase the costs of patient care including additional diagnostic tests and therapies, prolonged hospitalization and post-discharge complications [30, 31]. Higher rates of HAIs in LMICs are enhanced by issues such as poor hand hygiene due for instance to heavy workloads, issues with infrastructure including a lack of water and blocked and leaking sinks, as well as poorly positioned facilities [32].

Overall HAIs have an appreciable impact on patients, healthcare workers, healthcare practitioner, and national healthcare systems. Descriptive surveys remained a useful tool for assessing healthcare settings and might be helpful in interpreting major issues associated with patient care [33]. Despite recent systematic and other reviews concerning HAIs among LMICs including sub-Sahara African countries [4, 19, 20, 29, 34], we believe there is still an epidemiological gap because few resource-limited settings have accurate surveillance systems for monitoring HAIs, although this is improving [9]. This is important given the high rate of infectious diseases in LMICs including sub-Sahara Africa with its high rate of HIV, TB and malaria, misuse of antibiotics in hospitals and variable prevention strategies [32, 35-38]. Consequently, in order to provide a current summary on the prevalence of HAIs, we undertook an updated systematic review to assess the

prevalence of HAIs based on PPS, and to identify the type of infections and microorganisms responsible for HAIs to improve future care. This builds on our recent publication that reports high rates of HAIs in Pakistan [39]. This systematic review gathers evidences concerning the burden of HAI in both LMIC and HIC, which we hope will help decision makers and officials to develop a robust system to cope up with HAIs by investigating constraints linked to the surveillance of HAIs in healthcare settings as well as identify opportunities for improvement.

2. METHODS

A systematic review was conducted to explore point prevalence surveys for HAIs. The study protocol and methodology was designed according to preferred reporting items for systematic and meta-analysis (PRISMA) guidelines [40]. We aimed to detect point prevalence surveys worldwide focusing on the types of infections as well as microorganisms responsible for these various infections.

2.1 Data Sources

We retrieved relevant articles using PubMed, EBSCO, ProQuest, CINHAL and Scopus databases and published in English from 1995 to the present year (2019). A comprehensive grey literature review was also performed using Google Scholar, the World Health Organization and the website of the European Centre for Disease Prevention and Control in case we missed important references. The selected reference lists were subsequently analyzed. References of the selected articles were also retrieved and reviewed to again see if we had missed relevant articles from our initial search.

2.2 Search Strategy

Data were searched using the keywords “health-care associated infection”, “hospital-acquired infections”, “point prevalence”, “repeated prevalence”, “period prevalence”, “survey”, “hospital(s)”, “intensive care units” by using truncations and Boolean operators (“OR” “AND”) from 1995 until April 2018. The corresponding Medical Subject Heading (MeSH) terms for the above keywords were also tried. Abstracts and full-text articles were screened for eligibility by applying PICO (population, interventions, comparison, and outcomes) approach [40].

2.3 Inclusion and Exclusion Criteria

In this systematic review, there was no restriction on the age or gender of the patients in the studies. We included English language abstracts and full-text articles on HAIs reporting three types of infections as well as three most frequent microorganisms responsible for HAIs. We excluded articles not in English. Review articles, editorials, case reports, qualitative studies, dissertations, as well as articles reporting the same information in a different format or Journal were also excluded. Studies lacking information about the types of infections were also excluded.

2.4 Quality Assessment

The methodological quality of included articles was assessed independently by two investigators (ZS and FA). For quality assessment of included articles, Newcastle-Ottawa scale (NOS) was used [41-43]. This scale stratifies the methodological quality of papers into three subscales, i.e. selection, comparability and outcomes. Differences in assessments were debated and agreed following a discussion with the review authors (MAH and IR).

2.5 Data extraction

A data extraction form was developed. The items on the data extraction form were finalized after discussion amongst members of the research team. Extracted data included the authors, region, world bank ranking, settings, PPS methodology and protocol, population type, study duration, infected patients, most frequent types of infections and most frequent 3 types of microorganisms. Retrieved publications were subsequently filtered using the study inclusion and exclusion criteria by 2 independent reviewers. Data were extracted from eligible articles by assessing titles, abstracts, and full-text articles.

2.6 Outcomes

The primary outcomes of this review were to assess the world-wide prevalence of HAIs and to identify the types of infections and microorganism isolated responsible for HAIs. Such knowledge can be used to initiate pertinent activities in hospitals to improve the future management of patients in hospitals to reduce the prevalence of HAIs. The HAI case definitions were adopted from ECDC protocol [13]. As a result, HAI was defined as 'an infection occurring in a patient during the process of care in a hospital or other health care facility which was not present or incubating at the time of admission'. For the purposes of this protocol, an infection was defined as active on the day of the survey when: signs and symptoms were present on the date of the survey; OR signs and symptoms were no longer present but the patient was still receiving treatment for that infection on the date of the survey. An active infection was defined as healthcare-associated when: the onset of the signs and symptoms was on Day 3 of the current admission or later; OR the signs and symptoms of an active surgical site infection were present at admission or started before Day 3, and the surgical site infection occurred within 30 days of a surgical intervention.

3. RESULTS

3.1 Literature Research

The flow chart of the search and selection strategies of articles is illustrated in Figure 1. Through scientific and grey literature searches, after removal of duplicates (N=87), a total of 1212 articles were screened for eligibility. After screening, 290 articles were eligible for detailed assessment and the remaining articles not fulfilling the inclusion criteria (N=922) were excluded. Abstracts and full-text articles of 59 articles were not screened due to language restrictions; 87 articles did not provide sufficient data; 13 review articles were excluded and 64 articles did not mention the infection of interest. As a result, a total of 67 studies were subsequently included in the final analysis.

Insert Figure 1

The abstracts of these 67 studies, as well as full-text articles of point prevalence surveys of HAIs in adults and mixed populations, are summarized in Table 1, providing updated information on the type of infections and microorganisms. Table 2 summarizes the data on the pediatric population. Overall, 35 studies were conducted in Europe (33 studies on adults and 2 on pediatrics), 21 in Asia (19 studies on adults and 2 on pediatrics), 9 in America (5 studies on adults and 4 on pediatrics and 2 in Africa (adults), all reporting the proportion of overall HAIs in a mixed population of patients [11-14, 44-106]. The majority of point prevalence surveys were conducted in more than one hospital following the European Centre for Disease Control and Prevention (ECDC) protocol. Out of 21 studies conducted in Asia, six studies were undertaken in China [12, 76, 79, 80, 84, 85].

HAIs showed a higher prevalence in intensive care units compared to other wards. The highest prevalence of HAIs was recorded in a study conducted in adult ICU settings among 75 regions of Europe (51.3%) [68]. In Asian countries, a study conducted in Turkey reported the highest prevalence rate of HAIs (48.7%) in ICU patients [93]. Whereas, in case of complete hospital survey, the highest burden of HAIs was observed in one pediatric hospital of Russia (15.1%), followed by Ethiopia (14.8%) and Tunisia (14.3%). The HAI prevalence rate was 11.7% in North America [99, 106]. Gravel et al. performed a PPS among adult and pediatric patients separately in Canada showing a slightly higher prevalence rate of HAIs (10.4%) among adults in comparison to pediatric patients (8.0%) [11, 97]. A point prevalence study conducted in Ireland reported a higher HAI prevalence rate (4.3%) in long-term care facilities [49].The lowest burden of HAIs was seen in a study conducted in six hospitals in Greece (2.9%).

3.2 Comparison of HAIs in HI and LMICs

Of the 67 selected studies, 46 studies were undertaken in high-income countries (HIs), 12 studies in upper middle-income countries (UMICs), 8 studies were conducted in LMICs and only one study in low-income countries (LICs) [11-14, 44-106]. All point prevalence surveys of HAIs in HIs have been published since 1995. 41 of 46 studies reported a prevalence rate of <20. In LMICs, point prevalence surveys of HAIs have been published since 2005. Of eight studies, five studies reported a prevalence rate of <10% and all except one reported prevalence rate of >20%. ICU acquired infections are the most common and leading HAIs hospital-wide. In LMICs, the prevalence rate of HAIs in ICU admitted patients is <35% while in HIs the prevalence of HAIs exceeds 50% [65, 68, 75, 81, 103]. In our findings, the frequency of surgical site infections was significantly higher in LMICs when compared with the studies conducted in HIs [44, 61, 73, 83]. Acinetobacter species were responsible for HAIs in LMICs [81, 83, 87]. In HIs, E. coli appeared to be the major cause of HAIs [13, 45, 48, 52, 57].

3.3 Types of infections and microorganisms isolated in among pediatric patients

The majority of published studies emphasized more than one site of infection. Regarding the types of infections, the majority of studies included data on urinary tract infections, respiratory tract infections, bloodstream infections, and surgical site infections. Among European countries, blood-stream infections (52.6%) were one of the commonest types of infections among pediatric patient, followed by upper respiratory tract infections (45.0%) [102, 105]. Blood-stream infections (30.6%) in North America and pneumonia (65.2%) in Asia were the most frequent infections among pediatric patients [94, 103]. In the United States, *coagulase-negative Staphylococcus* (31.6% and 19.5%) was the major cause of HAIs, followed by *Enterococcus species* (10.3% and 12.2%) [104, 105]. *Klebsiella pneumonia*, *Pseudomonasaeroginosa*,and*Acinetobacter* species were the most frequent pathogens responsible for HAIs among Asian countries [14, 103].

3.4 Types of infections and microorganisms isolated in adults

In Africa, surgical site infections (51.1%) were the most frequent type of infection [99]. In Vietnam, there were high reported rates of lower respiratory tract infections in adults (79.4%), whereas in Italy reported high rates of bloodstream infections (50.0%) [55, 81]. Respiratory tract infections were the most frequent type of infections in patients admitted to ICUs (63.5%) and in patients admitted to long-term care facilities in Ireland (35.0%) [49, 68].

More than half of the HAIs infections are caused by gram-negative bacteria. Gram-negative pathogens such as *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *E. coli*, and *Acinetobacte*r species were the most frequently reported pathogens. Gram-positive pathogens such as *Staphylococcus aureus* and *clostridium difficile* were also included in these studies. *Staphylococcus aureus*, *Pseudomonas aeroginosa*, and *Klebsiella* species were the major cause of HAIs in Africa (20.4%, 18.3% and 22.4%) and South America the (21.6%, 12.5% and 19.2%) [98, 99].Gram-negative bacteria were responsible for the different types of healthcare-associated infections in European countries (52.7%) as well as in Asian countries (67.1%) [67, 80]. In ICUs patients, *AcinetobacterBaumannii* (24.4%) was the most common pathogen responsible for HAIs [81]. Other publications reporting types of infections as well as types of microorganism are listed in Tables 1 and 2.

Insert Tables 1 and 2.

3.5 Quality Assessment

The maximum of ten stars is awarded to a study. We considered study a high quality when scored ≥7, a medium quality scored 5-6 and a low quality scored 0-4. The stars that were awarded to studies ranged from six to nine, and the average value was 7.7 (Table 3). Most of the studies used ECDC protocol as a validated measurement tool to assess the prevalence of HAIs. Independent blind assessment was done in all studies.

Insert Table 3

4. DISCUSSION

Healthcare-associated infections are among the most serious public health issues with substantial morbidity, mortality and costs [3, 20, 107, 108]. We subsequently systematically reviewed sixty-seven studies reporting the proportion of overall HAIs in mixed patient populations. The selected studies conducted in various healthcare settings provide baseline information in order to develop future intervention research. Because of multi-factorial features of HAIs, healthcare settings are challenging domains in order to identify the various types of infections and microorganisms, especially in LMICs. Most of the studies were conducted in Europe and Asia. Two studies were conducted in Africa, one in Ethiopia and one in Tunisia. Previous literature surveys reported that HAIs remained a public health problem in LMICs compared with developed countries [29]. However, to date limited studies regarding PPS of HAIs have been performed in LMICs because of lack of national surveillance systems. The main reasons for this may include a lack of human and financial resources, the absence of expertise in interpretation of the data, the paucity of reliable diagnostic procedures, the scarcity of data obtained from patient records and the absence of software used for surveillance of HAIs [17].

In Canada, Denis et al conducted prevalence surveys in both adults and pediatric settings with reportedly a high prevalence rate of HAIs in adults than in pediatric patients. One of the studies reported a 3-20 times higher neonatal infection rate in developing countries compared to developed countries [28]. Rezende and colleagues performed a prevalence survey in Brazil and reported 11.4% prevalence of HAIs, requiring inter-institutional efforts so that appropriate measures could be taken. The frequency of endemic HAIs in neonatal ICUs in a few regions for example Brazil is 9 times higher than in USA [29]. The higher heterogeneity in the prevalence data may be due to

the different study design and the selection of participants, e.g., study populations, races, and sample sizes, among the reviewed studies. According to the WHO, the pooled prevalence of HAIs in LMICs was 10.1%, while in HIs the pooled prevalence of HAIs was 7.6% [34]. Due to insufficient data or lack of resources in LMICs, the pooled prevalence of HAIs was significantly higher in LMICs than in HIs.

Our findings indicated that lower respiratory tract infections are the leading HAIs followed by urinary tract infections, surgical site infections and bloodstream infections in most of the selected studies. A study performed in Australia reported high rates of illness from acute as well as chronic respiratory tract infections in the indigenous pediatric population [109]. This is important as pneumonia is the most frequent lower respiratory tract infection and a leading cause of death [110]. A study conducted in Ethiopia has reported high rates of surgical site infections. Surgical site infection leads to a prolonged hospital stay and increased costs of therapy [111]. In our findings, surgical site infections were the most frequent type of HAI in LMICs. This is similar to Allegranzi and his colleagues and the WHO who also reported surgical site infection as the most common type of HAI [17, 34]. Surgery and invasive procedures were among the significant risk factors responsible for surgical site infections (SSIs) [112]. To address concerns, the WHO have published their guidelines to ensure surgical patient's safety which includes a safety checklist to reduce mortality from SSIs [113].

The evaluation of microbiological patterns of HAIs was based on isolates of the three most frequent microorganisms. Gram-negative bacteria were reported as the principal causative pathogens in Europe and Asia [48, 57, 70, 80, 91, 93]. Our results reported that *Staphylococcus aureus*, *Pseudomonas aeroginosa*, and *Klebsiella* species were the most frequent pathogens in Africa and South America [99]. This is similar to a review in Africa where *Klebsiella*, *Staphylococcus aureus*, *Pseudomonas aeroginosa* and E coli were the most common organisms associated with healthcare-associated infections [114]. Six point prevalence studies conducted in China reported *Pseudomonas aeruginosa* as the leading cause of healthcare-associated infections [12, 76, 79, 80, 84, 85].

Overall, we believe our data provides significant information to guide policy makers to identify risk factors of HAIs and to devise prior strategies to reduce HAIs. In order to detect trends of HAIs, additional point prevalence surveys are needed, with the findings directing quality improvement programmes in hospitals. As part of this, proper instruction should be given to patients to identify and report signs and symptoms of HAIs. This intervention may help in the identification of HAIs during their hospital stay and after discharge. Moreover, prioritization of resources may help to prevent HAIs and improve patient's safety once specific activities have been identified [115]. Overall, patient participation is considered as an integral part of reducing medical error and improving patient's safety [116].We are aware that there will be different challenges to reduce HAIs between HIs and LMICs in line with the challenges to introduce effective antimicrobial stewardship programmes in LMICs and HIs [117]. This especially given the current lack of AMS programmes among a number of LMICs [118, 119]. Consequently, quality improvement programmes to reduce future HAIs must be tailored to the given country and situation.

Our study has limitations that should be kept in mind when elucidating data from selected studies. The current systematic review utilized five databases with specific emphasis on terms describing point prevalence surveys of healthcare-associated infections and hospital-acquired infections. Limited grey literature searches were also performed using additional search terms that identified

relevant articles. As a result, some relevant articles may have been missed. Moreover, only English language studies were retrieved resulting in the exclusion of studies in other languages. In some studies, available information was not explained enough such as lack of information on microorganisms. In other studies, the analysis performed by the authors was a mixture of HAI prevalence data on both intensive and acute care units. Considering higher HAI prevalence rates in intensive care units, it could influence the differences in results. Another limitation is that lower reported HA prevalence does not necessarily or even often mean lower true prevalence rates - overall diagnostic capabilities and reporting culture can play a surprisingly large role between countries and cultures, leading to large differences which can be misinterpreted. The difference in the quality of different countries' health-care systems and the definitions of infections had also a discernible influence on the systematic review. Lastly, we had divided studies into adults and pediatric population by considering total hospital population as adults. However, despite these limitations we believe our findings are robust providing direction to others.

5. CONCLUSION

The current systematic review provides an updated synthesis of literature concerning the overall burden of HAIs. These findings reported the existence of multiple pathogens responsible for healthcare associated infections in a variety of healthcare settings. Based on this literature review, standardized surveillance systems, infection prevention and control programs, multidisciplinary teams, instigation of antibiotic stewardship programmes, as well as the raising of awareness among medical staff and policy makers regarding HAIs and ways to prevent these may be effective strategies to minimize the future risk of HAIs. We recommend that more point prevalence surveys should be conducted in order to identify and target scarce resources for the prevention of future HAIs in all countries especially LMICs building on ongoing activities in these countries.

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TABLE 1. Point Prevalence Surveys in mixed population

Continent and Countries	World Bank Classification	Author Name and Date	Settings	PPS Method	PPS Protocol	Study Duration	HAIs (%)*	Top Three Types of Infections (%)*			Top Three types of microorganisms (%)		
EUROPE													
Poland [44]	HI	Deptula et al., 2017	160 ICUs	Period	ECDC, EU-PPS & AU	2012-2014	370/945 (39.1%)	Respiratory tract infections (45%)	Bloodstream infections (14%)	Surgical site infections (13%)	Acinetobacter baumannii (15.2%)	Pseudomonas aeruginosa (14.1%)	Klebsiella pneumoniae (14.1%)
Italy [45]	HI	Sticchi et al., 2017	18 hospitals	Period	ECDC	22 March-22 April 2016	376/3647 (10.3%)	Respiratory tract infections (21.7%)	Urinary tract infections (20.1%)	Bloodstream infections (16.8%)	E. coli (18.2%)	Klebseilla pneumonia (13.4%)	Coagulase negative staphylococcus (12.5%)
Switzerland [46]	HI	Swissnoso, 2017	96 hospitals	Period	ECDC	April-May 2017	763/12931 (5.9%)	Surgical site infections (29.0%)	Lower respiratory tract infections (18.0%)	Urinary tract infections (15.0%)	Enterobacteriaceae (45.7%)	Gram positive cocci (36.6%)	Gram negative bacteria (5.5%)
Slovenia [47]	HI	Klavs et al., 2016	21 hospitals	One day	ECDC	October 2011	358/5628 (6.3%)	Upper respiratory tract infections (21.5%)	Pneumonia (21.0%)	Surgical site infection (18.4%)	-	-	-
Austria [48]	HI	Lusignani et al., 2016	9 hospitals	Period	ECDC	May- June 2012	268/4321 (6.2%)	Urinary tract infections (21.3%)	Pneumonia (20.6%)	Surgical site infections (17.4%)	E.coli (10.5%)	Enterococcus species (13.1%)	Pseudomonas aeroginosa (11.4%)
Ireland [49]	HI	Roche et al., 2016	24 LTCFs	Period	ECDC & HPSC	May 2013	46/1060 (4.3%)	Respiratory tract infections (35.0%)	Skin infections (35.0%)	Urinary tract infections (12.0%)	-	-	-
Slovakia [50]	HI	Stefkovicova et al., 2015	40 hospital	Period	ECDC	June 2012	298/8397 (3.5%)	Urinary tract infections (26.2%)	Surgical site infections (15.7%)	Blood stream infections (9.9%)	E.coli. (15.0%)	Klebsiella species (12.5%)	Pseudomonas aeroginosa (10.8%)
France [51]	HI	Milliani et al., 2015	4 HCS	Period	France National PPS	14 May-21 June 2012	403/5954 (6.8%)	Urinary tract infections (26.6%)	Skin and soft tissue infections (17.6%)	Surgical site infections (15.0%)	Enterobacteiaceae (41.0%)	Gram positive cocci (40.0%)	Stapgylococcus aureus (21.0%)
19 Countries [53]	HI	Katrien et al., 2014	1181 LTCFs	Period	ECDC	April-May 2013	2626/77264 (3.4%)	Respiratory tract infections (31.2%)	Urinary tract infections (31.2%)	Skin infections (22.8%)	E. coli (34.4%)	Staphylococcus aureus (10.2%)	Proteus Mirabilis (8.1%)
28 Countries [52]	HI	Katrien et al., 2014	722 LCTF	Period	ECDC	May-September 2010	2495/61932 (4.0%)	Respiratory tract infections (33.6%)	Urinary tract infections (22.3%)	Skin infections (21.4%)	E.coli (38.3%)	Staphylococcus aureus (13.5%)	Proteus mirabilis (9.9%)
12 Countries [54]	HI	Erdam et al., 2014	88 ICUs	One day	CDC	Between June- July 2012 /one day	305/749 (40.7%)	Pneumonia (53.4%)	Bloodstream infections (18.3%)	Urinary tract infections (30.7%)	Gram negative bacilli (20.3%)	Acinetobacter species (15.4%)	Pseudomonas aeruginosa (9.5%)

Italy [55]	HI	Sinatra et al., 2013	3 departments	One day	ECDC	September 2011	12/328 (3.6%)	Blood stream infections (50.0%)	Urinary tract infections (28.5%)	-	-	-	-
Ireland [56]	HI	Smiddy et al., 2013	8 units	Period	Own	2006-2009	23/754 (3.0%)	Bloodstream infections (25.0%)	Surgical site infections (25.0%)	Urinary tract infections (20.8%)	-	-	-
Germany [57]	HI	Behnke et al., 2013	132 hospitals	Period	ECDC	September-October 2011	2109/41539 (5.1%)	Surgical site infections (24.3%)	Urinary tract infections (23.2%)	Respiratory tract infections (21.7%)	E.coli (18.0%)	Enterococci (13.2%)	Staphylococcus aureus (13.1%)
33 Countries [58]	HI	Carl Suetens et al., 2013	947 hospitals	Period	ECDC	2011-2012	13829/231459 (5.9%)	Respiratory tract infections (23.5%)	Surgical site infections (19.6%)	Urinary tract infections (19.0%)	E. coli (15.9%)	Staphylococcus aureus (12.3%)	Enterococcus species (9.6%)
23 Countries [13]	HI	Zarb et al., 2012	66 hospitals	Period	ECDC	May 2010-October 2010	1408/19888 (7.0%)	Pneumonia (25.7%)	Surgical site infections (18.9%)	Urinary tract infections (17.2%)	E. coli (15.2%)	Staphylococcus aureus (12.1%)	Pseudomonas aeroginosa (11.2%)
Germany [59]	HI	Heudorf et al., 2012	40 nursing homes	Period	HALT	January 5,-Mach 9, 2011	161/3732 (4.3%)	Urinary tract infections (28.0%)	Respiratory tract infections (25.5%)	Skin infections (15.5%)	-	-	-
London [60]	HI	Coello et al., 2011	5 hospitals	Period	ESAC	July 2009	104/1354 (7.7%)	Surgical site infections (18.2%)	Urinary tract infections (18.2%)	Bloodstream infections (14.0%)	-	-	-
France [61]	HI	Lietard et al., 2011	2337 healthcare facilities	One day	CDC	2006	12182/199716 (6.1%)	Urinary tract infections (2.4%)	Pneumonia (2.4%)	Surgical site infections (0.8%)	E.coli (28%)	Staphylococcus aureus (18.2%)	Pseudomonas aeruginosa (9.5%)
Greece [62]	HI	Alexopoulos et al., 2011	6 hospitals	One day	CDC	December 2005-February 2006	64/2180 (2.9%)	Urinary tract infections (34.2%)	Lower respiratory tract infections (14.3%)	Bloodstream infections (14.3%)	E. coli (14.3%)	Pseudomonas areuginosa (10%)	Enterococcus species (8.6%)
England [63]	HI	Hopkins et al., 2011	103 organization	Period	ECDC	September-November 2011	3360/52443 (6.4%)	Respiratory tract infections (22.8%)	Urinary tract infections (17.2%)	Surgical site infections (15.7%)	Enterobacteriaciae (14.1%)	Staphylococcus aureus (6.7%)	Closridium difficile (5.4%)
Scotland [64]	HI	Cairns et al., 2011	45 hospital	Period	CDC	2005-2006	1094/11090 (9.8%)	Urinary tract infections (17.9%)	Surgical site infections (15.7%)	Gastrointestinal infections (15.5%)	-	-	-
Scotland [65]	HI	Cairns et al., 2010	29 ICUs	Period	Own	October 2005-September 2006	35/129 (27.1%)	Lower respiratory tract infections (23.9%)	Surgical site infections (23.9%)	Pneumonia (19.5%)	-	-	-
Belgium [66]	HI	Gordts et al., 2010	63 hospitals	Period	CDC	October – November 2007	1037/17343 (5.9%)	Urinary tract infections (23.9%)	Lower respiratory tract infections (20.0%)	Surgical site infections (14.6%)	-	-	-

Italy [67]	HI	Lanini et al., 2009	51 hospitals	Period	CDC	2002-2004	589/9609 (6.1%)	Lower respiratory tract infections (35.8%)	Urinary tract infections (23.6%)	Bloodstream infections (14.0%)	Gram negative bacteria (52.7%)	Gram positive bacteria (38.8%)	Fungi (5.0%)
75 Countries [68]	HI	Vincet et al., 2009	1265 ICUs	One day	CDC	2006-2007	7087/13796 (51.3%)	Respiratory tract infections (63.5%)	Abdominal infections (19.6%)	Bloodstream infections (15.0%)	Staphylococcus aureus (20.5%)	E .coli (16.0%)	Pseudomonas species (19.9%)
France [69]	HI	Patte et al., 2005	Homecare Setting (HCS)	One day	Own	June 5, 2000	23/376 (6.1%)	Urinary Tract Infections (50.0%)	Skin Infections (37.9%)	-	E. coli (29.4%)	Staphylococcus aureus (29.4%)	Enterococcus species (17.6%)
Italy [70]	HI	Lizioli et al., 2003	88 hospitals	Period	Own	February-March 2000	916/18667 (4.9%)	Urinary tract infections (33.6%)	Pneumonia (22.6%)	Surgical site infections (15.0%)	E.coli (16.8%)	Staphylococcus aureus (15.0%)	Pseudomonas aeruginosa (13.2%)
Greece [71]	HI	Starakis et al., 2002	19 units	Period	CDC	1998 and 1999	97/997 (9.7%)	Lower respiratory tract infections (36.0%)	Urinary tract infections (25.8%)	Bloodstream infections (19.6%)	Pseudomonas aeroginosa (20.6%)	Kelbsiella pneumonia (8.2%)	Staphylococcus (7.2%)
Greece [72]	HI	Gikas et al., 2002	14 hospitals	One day	CDC	November 16, 1999	337/3925 (8.6%)	Lower respiratory tract infections (30.3%)	Urinary tract infections (22.7%)	Bloodstream infections (15.8%)	Pseudomonas aeroginosa (16.6%)	E. coli (10.8%)	Klebsiella pneumoniae (10.3%)
France [73]	HI	Group et al., 2000	830 hospitals	Period	Own	May 20 - June 21 1996	15798/2363 34 (6.7%)	Urinary tract infections (0.19%)	Lower respiratory tract infections (0.07%)	Surgical site infections (0.06%)	E. coli (20%)	Staphylococcus aureus (16%)	Pseudomonas aeroginosa (11%)
Switzerland [74]	HI	Pittet et al., 1999	4 hospitals	One week	CDC	May 1996	156/1349 (11.6%)	Surgical site infections (30.0%)	Urinary tract infections (22.0%)	Respiratory tract infections (15.0%)	Enterobacteriaceae (28.0%)	Staphylococcus aureus (13.0%)	Pseudomonas aeruginosa (11.0%)
17 Countries [75]	HI	Vincent et al., 1995	1417 ICUs	One day	Own	April 28-April 29, 1992	4501/10038 (44.8%)	Pneumonia (46.9%)	Lower respiratory tract infections (17.8%)	Urinary tract infections (17.6%)	Enterobacteriaceae (34.4%)	Staphylococcus aureus (30.1%)	Pseudomonas aeroginosa (28.7%)
ASIA													
China [76]	UMI	Chen et al., 2017	52 hospitals	One day	NHFPC	October 2014-March 2015	1998/53939 (3.7%)	Lower respiratory tract infections (47.2%)	Urinary tract infections (12.3%)	Upper respiratory tract infections (11.0%)	Pseudomonas aeroginosa (9.4%)	Acinetobacter Baumanni (7.9%)	Klebsiellapnuemoniae (7.3%)
India [77]	LMI	Nair et al., 2017	1 hospital	Period	CDC	March 2014-August 2014	71/1886 (3.7%)	Surgical site infections (23.9%)	Pneumonia (18.3%)	Upper respiratory tract infections	-	-	-

										(16.9%)			
Singapore [78]	HI	Cai et al., 2017	13 hospitals	Period	ECDC	July 2015-February 2016	646/5415 (11.9%)	Clinical sepsis (25.5%)	Pneumonia (24.8%)	-	Staphylococcus aureus (12.9%)	Pseudomonas aeroginosa (11.5%)	-
China [79]	UMI	Liu et al., 2016	124 hospitals	One day	BNICC	May 2014	1294/61990 (2.0%)	Urinary tract infections (15.0%)	Gastrointestinal infections (7.7%)	Surgical site infections (6.3%)	Pseudomonas aeruginosa (13.8%)	Acinetobacter baumannii (12.9%)	E.Coli (12.6%)
China [80]	UMI	Zhang et al., 2016	43 clinical departments	Period	CDC	May 2012-May 2014	147/4029 (3.6%)	Respiratory tract infections (54.8%)	Urinary tract infections (21.4%)	Blood stream infections (7.1%)	Gram negative bacteria (67.1%)	Gram positive bacteria (20.3%)	Fungi (10.5%)
Vietnam [81]	LMI	Phu et al., 2016	14 ICUs	One day each month	ECDC	October 2012-October 2013	965/3266 (29.5%)	Lower respiratory tract infections and pneumonia (79.4%)	Bloodstream infections (4.4%)	Surgical site infections (4.2%)	Acinetobacter baumannii (24.4%)	Pseudomonas aeroginosa (13.8%)	Klebsiella pneumoniae (11.6%)
Japan [82]	HI	Morioka et al., 2015	1 Hospital	One day	ECDC	July 3, 2014	85/841 (10.1%)	Pneumonia (20.0%)	Surgical site infections (19.0%)	Blood stream infections (11.1%)	Enterobacteriaceae (27.6%)	Staphylococcus aureus (15.5%)	Enterococcuss (10.3%)
India [83]	LMI	Kumar et al., 2014	1 Hospital	One day	CDC	2008 and 2011	125/1834 (6.8%)	Surgical site infections (33.0%)	Upper respiratory tract infections (26.0%)	Pneumonia (24.0%)	Klebsiella pneumonia (15.0%)	Pseudomonas aeruginosa (15.0%)	Acinetobactercal cobaumanni (2.4%)
China [84]	UMI	Tao et al., 2014	48 wards	One day	US CDC	November 13,2013	86/2434 (3.5%)	Respiratory tract infections (49.4%)	Surgical Site infections (22.9%)	Gastrointestinal infections (9.2%)	Pseudomonas aeruginosa (24.0%)	Klebseilla pneumonia (14.0%)	E. coli (14.0%)
China [85]	UMI	Xie et al., 2013	5 departments	Period	NISS	2007-2011	287/9533 (3.0%)	Respiratory tract infections (74.1%)	Urinary tract infections (8.9%)	Surgical site infections (5.9%)	Pseudomonas aeruginosa (10.4%)	E.coli (5.9%)	Acinetobacter baumannii (5.9%)
Iran [86]	UMI	Askarian et al., 2012	8 hospitals	Period	NNIS	2008-2009	323/3450 (9.4%)	Bloodstream infections (26.6%)	Surgical site infections (25.7%)	Urinary tract infections (14.9%)	-	-	-
Vietnam [87]	LMI	Thu et al., 2011	36 hospitals	Period	CDC	February 2008-December 2009	553/7571 (7.3%)	Pneumonia (41.9%)	Surgical site infections (27.5%)	-	Pseudomonas aeruginosa (31.5%)	Acinetobacter baumannii (23.3%)	-
Mongolia[88]	LMI	Ider et al., 2010	2 hospitals	One day	US CDC	September 2008	50/933 (5.3%)	Respiratory tract infections (24%)	Urinary tract infections (20%)	Surgical site infections (20%)	-	-	-

China [12]	UMI	Xie et al., 2010	13 hospitals	Period	CDC	November, 2007-November, 2008	790/20350 (3.9%)	Respiratory tract infections (63.1%)	Surgical site infections (9.6%)	Urinary tract infections (8.6%)	Pseudomonas aeruginosa (16.4%)	E.coli (10.5%)	Klebsiella pneumoniae (7.9%)
Hong Kong [89]	HI	Lee et al., 2007	1 hospital	One day	CDC	September 7,2005	41/1021 (4.0%)	Pneumonia (33%)	Surgical site infections (26.2%)	Bloodstream infections (21.4%)	Pseudomonas aeroginosa (N/A)	Staphylococcus aureus (N/A)	-
Saudi Arabia [90]	HI	Balkhy et al., 2006	7 units	One day	Own	May 2003	38/562 (6.7%)	Bloodstream infections (31.1%)	Ventilator acquired pneumonia (28.9%)	Urinary tract infections (24.4%)	Pseudomonas species (20.9%)	Enterococcuss species (18.9%)	Klebsiella pneumoniae (13.7%)
Thailand [91]	LMI	Danchaivijitr et al., 2005	42 hospitals	Two week	Own	March 12-March 25 2001	1181/18456 (6.4%)	Lower respiratory tract infections (34.0%)	Urinary tract infections (21.5%)	Surgical site infections (15.0%)	Pseudomonas aeruginosa (19.8%)	Klebsiella pneumonia (13.5%)	Acinetobacter species (13.0%)
Malaysia [92]	UMI	Hughes et al., 2005	5 clinical departments	Period	CDC	July 16-17, 2001	75/538 (13.9%)	Clinical sepsis (22.4%)	Pneumonia (21.4%)	Urinary tract infections (12.2%)	Pseudomonas aeruginosa (17.4%)	MRSA (15.5%)	MSSA (8.7%)
Turkey [93]	UMI	Esen et al., 2004	56 ICUs	One day	CDC	September 19, 2001	115/236 (48.7%)	Pneumonia (28.0%)	Blood stream infections (23.3%)	Urinary tract infections (15.7%)	Pseudomonas aeroginosa (20.8%)	Staphylococcus aureus (18.2%)	Acinetobacter species (18.2%)
AMERICAs													
Canada [106]	HI	Taylor et al., 2016	49 hospitals	One day	NHSN	February 2009	1173/9953 (11.7%)	Urinary tract infections (34.8%)	Pneumonia (21.8%)	Surgical site Infections (17.4%)	-	-	-
Florida [95]	HI	Magill et al., 2012	9 hospitals	One day	NHSN	August 2009	51/851 (6.0%)	Surgical site infections (31.0%)	Pneumonia (15.5%)	Urinary tract infections (15.5%)	Staphylococcus aureus (15.5%)	Candida species (10.3%)	Pseudomonas aeruginosa (8.6%)
USA [96]	HI	Magill et al., 2014	183 hospitals	One day	NHSN	May-September 2011	452/11282 (4.0%)	Pneumonia (21.8%)	Surgical site infections (21.8%)	Gastrointestinal infections (17.1%)	Clostridium difficile (12.1%)	Staphylococcus aureus (10.7%)	Klebsiella pneumonia (9.9%)
Canada [97]	HI	Gravel et al., 2007	25 hospitals	Period	CDC	February 5 – February 8 2001	601/5750 (10.4%)	Urinary tract infections (3.4%)	Pneumonia (3.0%)	Surgical site infections (2.5%)	Coagulase negative staphylococcus (N/A)	Gram negative bacteria (N/A)	Gram positive bacteria (N/A)
Brazil [98]	UMI	Rezende et al., 1998	11 hospitals	Period	CDC & NNIS	August – October 1992	267/ 2339 (11.4%)	Pneumonia (19.5%)	Surgical site infections (19.2%)	Urinary tract infections (13.1%)	Staphylococcus aureus (21.6%)	E.coli (21.6%)	Pseudomonas species (12.5%)
AFRICA													
Ethiopia [99]	LI	Yallew et al., 2016	2 hospitals	Period	CDC	March-July 2015	135/908 (14.8%)	Surgical site infections (51.1%)	Pneumonia (25.0%)	Blood stream infections (19.0%)	Klebseilla species (22.4%)	Staphylococcus aureus (20.4%)	Pseudomonas aeruginosa (18.3%)
Tunisia [100]	LMI	Kallel et al., 2005	15 departments	One day	Own	April 17-april 18 2002	50/280 (14.3%)	Pneumonia (32.0%)	Surgical site infections (28.0%)	Urinary tract infections (20.0%)	Klebsiella pneumoniae (23.1%)	Pseudomonas aeroginosa (19.2%)	Acinetobacterbaumannii (15.4%)

*Percentages of total infections, E.coli= Escherichia coli, N/A= Not Available, LMI= low middle income and low income country, HI= High Income country, UMI= Upper middle income country, CDC= Centre for Disease Prevention and Control, ECDC= European Centre for Disease Prevention and Control, NHSN= National Healthcare Safety Network, HELICS= Hospital in Europe Link for Infection Control through Surveillance, EU-PPS-AU= Europe Union Point Prevalence Surveys and Antibiotic Use Protocol, HPSC= Health Protection Surveillance Centre, HALT= Healthcare associated infections in Long Term care Facilities project, ESAC= European Surveillance of Antibiotic consumption, NHFPC= National Health and Family Planning Commission Centre, BNICC= Beijing Nosocomial infection Surveillance system,

TABLE 2. Point Prevalence Surveys in Pediatrics

Continent and Countries	World Bank Classification	Author Name and Date	Settings	PPS Method	PPS Protocol	Study Duration	HAIs (%)*	Top Three Types of Infections (%)*			Top Three types of microorganisms (%)		
EUROPE													
29 Countries [101]	HI	Zingget al., 2017	1149 hospitals	Period	ECDC	May 2011-November 2012	726/17273 (4.2%)	Bloodstream infections (45%)	Lower respiratory infections (22.0%)	Gastronintestinal infection (8.0%)	Enterobacteriacea (15.0%)	-	-
Russia [102]	UMI	Hajdu et al., 2007	1 hospital	One day	HELICS	February 2006	60/395 (15.1%)	Upper respiratory tract infections (45.0%)	Lower respiratory tract infections (19.0%)	Urinary tract infections (12.0%)	-	-	-
ASIA													
Vietnam [103]	LMI	Le et al., 2016	ICUs	One day/once in a month	ECDC	October 2012-September 2013	454/1363 (33.3%)	Pneumonia (65.2%)	Blood stream infections (26.1%)	Surgical site infections (2.0%)	Klebseilla pneumonia (19.0%)	Pseudomonas species (18.0%)	Acinetobacter species (15.0%)
Turkey [14]	UMI	Kepenekliet al., 2015	50 ICUs	One day	CDC	September 2012	122/327 (37.3%)	Lower respiratory tract infections (55.3%)	Blood stream infections (27.3%)	Urinary tract infections (7.1%)	Pseudomonas aeruginosa (24.0%)	Acinetobacter species (15.0%)	Candida species (7.0%)
AMERICA													
Canada [94]	HI	Rutledge-Taylor et al., 2012	30 hospitals	One day	CDC	February 3, 2009	118/1353 (8.7%)	Bloodstream infections (30.6%)	Pneumonia (16.1%)	Viral gastroenteritis (13.7%)	Coagulase negative staphylococcus (47.4%)	Pseudomonas aeroginosa (35.0%)	Candida species (30.8%)
Canada [11]	HI	Gravel et al., 2007	25 hospitals	One day	CNISP	February 5 – February 8 2001	80/997 (8.0%)	Blood stream infections (37.5%)	Pneumonia (26.2%)	Urinary tract infections (12.5%)	Coagulase negative staphylococcus (NA)	Gram negative bacteria (NA)	Gram positive bacteria (NA)
US [104]	HI	Grohskopfet al., 2002	31 hospitals	One day	Own	August 1999	61/512 (11.9%)	Bloodstream infections (41.3%)	Respiratory tract infections (22.6%)	Urinary tract infections (13.3%)	Coagulase negative staphylococcus (19.5%)	Enterococcus (12.2%)	Staphylococcus aureus (11.0%)
US [105]	HI	Sohn et al., 2001	29 Neonatal intensive care units	One day	Own	August 9, 2000	94/827 (11.3%)	Bloodstream infections (52.6%)	Respiratory tract infections (12.9%)	Urinary tract infections (8.6%)	Coagulase negative staphylococcus (31.6%)	Enterococci (10.3%)	E.coli (8.5%)

*Percentages of total infections, E.coli= Escherichia coli, N/A= Not Available, LMI= low and low middle income country, HI= High Income country, UMI= Upper middle income country, , CDC= Centre for Disease Prevention and Control, ECDC= European Centre for Disease Prevention and Control, HELICS= Hospital in Europe Link for Infection Control through Surveillance, CNISP= Canadian Nosocomial Infection Surveillance Programs

Table 3. Quality assessment of included articles

	Selection				Comparability	Outcomes		
Studies	**Representatives of sample[A]**	**Sample size[B]**	**Non-respondents[C]**	**Ascertainment of exposure[D]**	**Based on design and analysis[E]**	**Assessment of outcomes[F]**	**Statistical test[G]**	**Quality score**
Deptula et al., 2017 [44]	*	*	-	*	**	**	*	8
Sticchi et al., 2017 [45]	*	*	-	*	**	**	*	8
Swissnoso, 2017 [46]	*	*	-	*	**	**	*	8
Klavs et al., 2016 [47]	*	*	-	**	*	**	*	8
Lusignani et al., 2016 [48]	*	*	-	*	**	**	-	7
Roche et al., 2016 [49]	*	*	-	*	*	**	-	6
Stefkovicova et al., 2015 [50]	*	*	-	*	**	**	-	7
Milliani et al., 2015 [51]	*	*	-	*	**	**	*	8
Katrien et al., 2014[53]	*	*	-	**	**	**	-	8
Katrien et al., 2014[52]	*	*	-	**	**	**	*	9
Erdam et al., 2014[54]	*	*	-	*	**	**	*	8
Sinatra et al., 2013 [55]	*	*	-	*	*	**	*	7
Smiddy et al., 2013 [56]	*	*	-	*	*	**	*	7
Behnke et al., 2013 [57]	*	*	-	**	**	**	*	9
Carl Suetens et al., 2013[58]	*	*	-	**	**	**	*	9
Zarb et al., 2012[13]	*	*	-	*	**	**	*	8
Heudorf et al., 2012 [59]	*	*	-	*	*	**	*	7
Coello et al., 2011 [60]	*	*	-	*	*	**	-	6

Lietard et al., 2011 [61]	*	*	-	*	**	**	-	7
Alexopoulos et al., 2011 [62]	*	*	-	*	**	**	-	7
Hopkins et al., 2011 [63]	*	*	-	*	**	**	*	8
Cairns et al., 2011 [64]	*	*	-	*	*	**	*	7
Cairns et al., 2010 [65]	*	*	-	*	*	**	*	7
Gordts et al., 2010 [66]	*	*	-	**	*	**	*	8
Lanini et al., 2009 [67]	*	*	-	*	**	**	*	8
Vincet et al., 2009[68]	*	*	-	*	**	**	*	8
Patte et al., 2005 [69]	*	*	-	*	*	**	*	7
Lizioli et al., 2003 [70]	*	*	-	*	**	**	-	7
Starakis et al., 2002 [71]	*	*	-	*	**	**	-	7
Gikas et al., 2002[72]	*	*	-	**	*	**	*	9
Group et al., 2000 [73]	*	*	-	**	**	**	*	9
Pittet et al., 1999[74]	*	*	-	**	**	**	*	9
Vincent et al., 1995[75]	*	*	-	**	**	**	-	8
Chen et al., 2017 [76]	*	*	-	*	**	**	*	8
Nair et al., 2017 [77]	*	*	-	**	*	**	*	8
Cai et al., 2017 [78]	*	*	-	*	*	**	*	7
Liu et al., 2016 [79]	*	*	-	**	**	**	*	9
Zhang et al., 2016 [80]	*	*	-	*	**	**	*	8
Phu et al., 2016 [81]	*	*	-	*	**	**	*	8
Morioka et al., 2015 [82]	*	*	-	**	**	**	*	9

Kumar et al., 2014 [83]	*	*	-	*	**	**	-	7
Tao et al., 2014 [84]	*	*	-	**	**	**	*	9
Xie et al., 2013 [85]	*	*	-	*	**	**	*	8
Askarian et al., 2012 [86]	*	*	-	*	*	**	*	7
Thu et al., 2011 [87]	*	*	-	**	*	**	*	8
Ider et al., 2010[88]	*	*	-	*	*	**	*	7
Xie et al., 2010[12]	*	*	-	*	**	**	*	8
Lee et al., 2007[89]	*	*	-	*	*	**	*	7
Balkhy et al., 2006[90]	*	*	-	*	**	**	*	8
Danchaivijitret al., 2005 [91]	*	*	-	*	**	**	-	7
Hughes et al., 2005 [92]	*	*	-	**	**	**	*	9
Esen et al., 2004 [93]	*	*	-	*	**	**	*	8
Taylor et al., 2016 [106]	*	*	-	*	*	**	*	7
Magill et al., 2012 [95]	*	*	-	*	**	**	*	8
Magill et al., 2014 [96]	*	*	-	*	**	**	*	8
Gravel et al., 2007[97]	*	*	-	*	**	**	*	8
Rezende et al., 1998 [98]	*	*	-	*	**	**	*	8
Yallew et al., 2016 [99]	*	*	-	**	**	**	*	9
Kallel et al., 2005 [100]	*	*	-	*	**	**	*	8
Zingg et al., 2017[101]	*	*	-	*	*	**	*	7
Hajdu et al., 2007 [102]	*	*	-	*	*	**	*	7
Le et al., 2016 [103]	*	*	-	*	**	**	*	8

Kepenekli et al., 2015 [14]	*	*	-	*	**	**	*	8
Rutledge-Taylor et al., 2012 [94]	*	*	-	*	**	**	*	8
Gravel et al., 2007[11]	*	*	-	*	**	**	*	8
Grohskopf et al., 2002 [104]	*	*	-	*	**	**	*	8
Sohn et al., 2001 [105]	*	*	-	*	**	**	*	8

A: *= truly representative of average in target population or somewhat representative of average in target population
B: *=justified or satisfactory, -- = not justified
C: *=satisfactory response rate, --= unsatisfactory or no description
D: **=validated measurement tool, *=non validated measurement tool, --= no description of measurement tool
E: **=confounding factors, *incomplete information, --= no information
F: **=independent blinded assessment or record linkage, *=self-report, --= no description
G: *=Yes, --=No

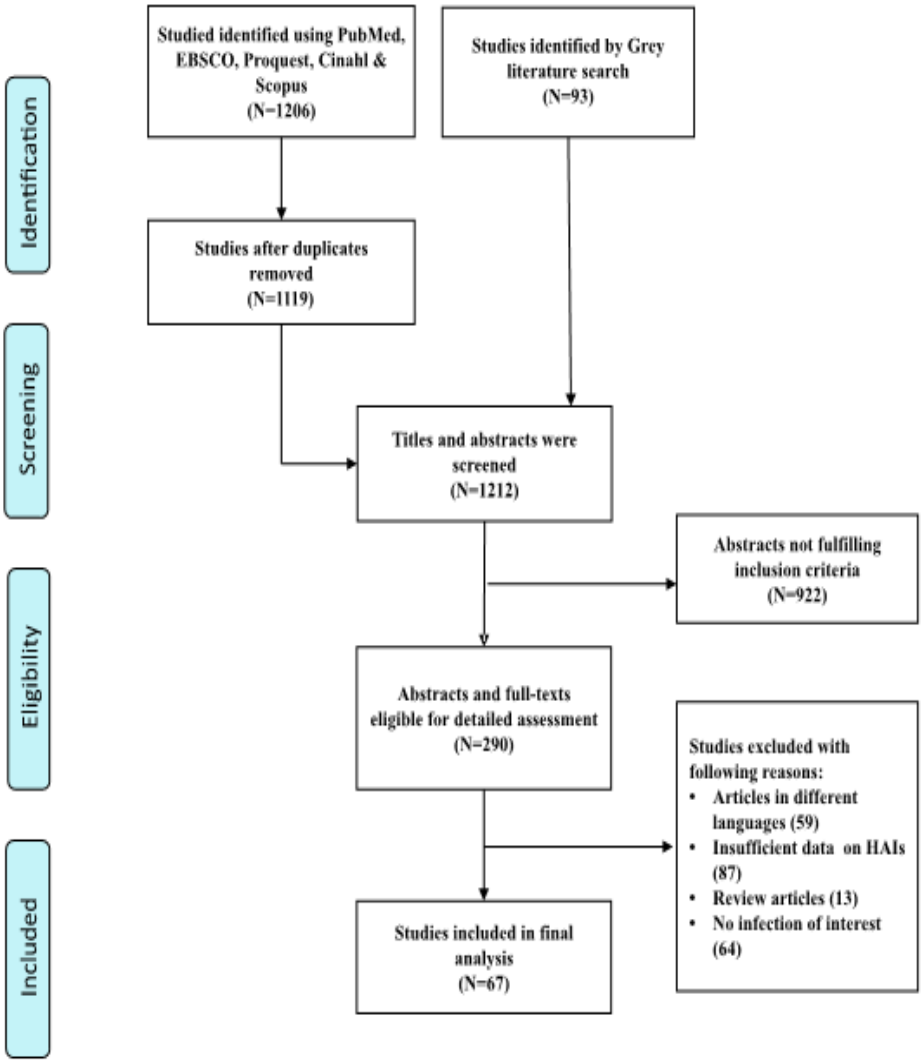

Figure 1. Flow chart and selection strategies of studies.